EXHIBIT C

EXPERT REPORT

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Among the lead authors of this paper, entitled *NOAC monitoring, reversal agents, and post-approval safety and effectiveness evaluation: A cardiac safety research consortium think tank,* is Dr. Paul Reilly, a BI scientist, a fact that reinforces not only the significance of the information, but the imputed knowledge to BI that a blood plasma concentration "sweet spot" to maximize stroke prevention and minimize excessive bleed risk is both known and capable of being measured. See, e.g., BIPI-PRA-0064015003 at. p.15.

101. Although I am not an expert on the regulation of pharmaceuticals by the European Medicines Agency (EMA), there are many European (EU) documents that are informative to the U.S. regulatory community. For example, I note that the CSRC's consensus statement is consistent with BI's internal discussions and the EMA's findings that given the dose response between Pradaxa and bleeding, there is likely a therapeutic range in which the risk reduction of ischemic stroke is maximized while the risk of a major bleed is simultaneously minimized. Another example of relevant information to my opinion is the EMA assessment report reflecting BI's determination that there is a 200 ng/ml cut off above which there is an excessive bleeding risk.[25]

102. BI stated in the EU Summary of Product Characteristics that:

> Pradaxa does not in general require routine anticoagulant monitoring. However, ***the measurement of dabigatran related anticoagulation may be helpful to avoid excessive high exposure to dabigatran*** in the presence of additional risk factors. The INR test is unreliable in patients on Pradaxa and false positive INR elevations have been reported. Therefore INR tests should not be performed. Diluted thrombin time (dTT), ecarin clotting time (ECT) and activated partial thromboplastin time (aPTT) may provide

[25] See, e.g., BIPI-PRA-0004609848 and BIPI-PRA-0004576462: "The MAH [BI] identified dabigatran concentrations not to be exceeded because of bleeding or in some special situations such as pre-surgical situations. The 215 ng/mL concentration is the value at trough (10-16 hours after previous dose), not to be exceeded because of the increased risk of bleeding."

245. This failure to complete the investigation of the need for a 110 mg dose that BI itself identified, i.e., for patients at excessive bleeding risk on the 150 mg dose, together with the refusal to conduct a large, randomized trial to find out whether safety – and therefore the corresponding benefit-risk assessment – could be improved, supports my opinion that BI has failed to adequately study and investigate its drug product as required by FDA regulations, industry standards and the obligations of what a reasonable drug company would do under these circumstances.

XIII. THE DEVELOPMENT OF PRAXBIND COULD HAVE ACCOMPANIED THE ORIGINAL MARKETING OF PRADAXA

246. BI identified mouse antibodies to dabigatran in 2002 and the antibody process used in Praxbind was therefore identified ***prior*** to Pradaxa approval. Significantly thereafter, the antibodies used to create Praxbind were finalized in a matter of months after initiation of the reversal agent research in 2008, and the 2002 antibody was "humanized" in 2009.[71] The bottom line is that the antibody that ultimately became Praxbind had been “on the shelf” for nearly six years when it was rediscovered in 2008 – well in advance of the market authorization to sell Pradaxa.[72]

Q. Right. What they wanted was to have some of the pathways that they had identified for the 110-milligram dose approval to be followed, right?

A. They wanted us to generate additional data, do a new study.

[71] Joann an Ryn depo, June 26, 2017 at 52:16 to 54:7.

[72] Significantly, Dr. Paul Reilly, a senior scientist at BI and global clinical lead for development of Praxbind (idarucizumab), the reversal agent for Pradaxa, was asked at his January 27, 2017 deposition about the timing of Praxbind development at 211:14 to 212:5 (emphasis added):

Q. So who at your company figured out they could use this process with the hamster ovary cells to make what turns out to be Praxbind?

*A. Well, I think the first insight **goes back to 2008** when our pharmacologist [NAME REDACTED] was at a conference and the issue of reversal agents or antidotes came up, and it occurred to her that **we had monoclonal antibodies on the shelf that we had already produced to dabigatran** and that may be utilized in a novel way to use as a way to neutralize the dabigatran effects, and that was -- she started in 2008 and*

334. BI's own records outline the decision not to develop a method to measure dabigatran plasma concentrations so as to maintain a competitive advantage in the marketplace, with doctors and patients, with institutions and with insurance companies/drug formularies.

335. BI did not warn or instruct physicians and patients to measure dabigatran plasma concentrations in an effort to maintain a competitive advantage in the marketplace, with doctors and patients, with institutions and with insurance companies/drug formularies.

336. BI brought Pradaxa to market before completing development of Praxbind, despite the early identification of the antibodies that ultimately became the reversal agent, such that Pradaxa patients were exposed to unnecessary risks of bleeding for which there was no specific reversal agent.

337. BI's design, manufacture and sale of Pradaxa without a reversal agent, despite the feasibility of developing a reversal agent at or about the time of Pradaxa product launch, exposed Pradaxa patients to unnecessary risks of bleeding.

338. BI's failures as set forth in this report, and specifically paragraphs 310 to 337, support my conclusions to a reasonable degree of pharmaceutical regulatory certainty that BI failed to meet its obligations as a drug sponsor to properly (a) investigate and study the risks and benefits of its product, (b) communicate the risks and benefits of Pradaxa, (c) instruct on ways to minimize Pradaxa's risks without unduly minimizing the benefits, and (d) provide honest and balanced information concerning Pradaxa's risks and benefits to medical/scientific community, physicians and patients. https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm355270.htm

351. As a physician, I state to a reasonably degree of medical certainty my opinion that Pradaxa can turn clinically insignificant gastrointestinal tract malformations, fissures and lesions into major, life threatening or fatal GI bleeds.

I hereby affix my signature to this report and the accompanying appendixes and schedules referenced herein.

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